EXHIBIT 1

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DRAFT – For Discussion Purposes Only

Expert Opinion Report

Quality Assurance & FDA Compliance

Actavis Inc.

Makers of Digitek

By

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1 – January – 2010

Summary of the Opinion

The SpyGlass Group, Inc. has determined that Actavis/Amide (hereafter referred to Actavis) was not complying with the FDA legal requirements for current Good Manufacturing Practice (cGMP or GMP) for at least the period of time, starting in 12/1/2004 and ending with their Permanent Injunction of Nov. 14, 2008. During this period of time, the records demonstrate that Actavis released product that did not meet product specification and as such were adulterated. Because of the serious violations of GMP, for this period of time, the production, control and quality processes for Digitek were not able to consistently and reliably manufacture products that meet legal requirements.

Their troubled past included a 1992 FDA Consent Decree. Then there was some period of time (1993 through the 1st Quarter of 2004) when FDA records indicate that the operations were GMP compliant. There were several FDA adverse findings notices (commonly called FDA 483) issued over this period of time; however, Actavis/Amide corrective action appeared to have satisfied the FDA's concerns. Then for a period of six (6) years, beginning in 2004 until their 2009 Permanent Injunction, there appears to have been a significant breakdown in their Quality Systems and overall compliance to GMP. As a result of multiple FDA site inspections over this six (6) year period, Actavis was issued multiple FDA adverse finding reports As a result of not taking swift and effective corrective action to the FDA 483s, the FDA escalated their public concern by issuing numerous FDA Warning Letters. Actavis did not effectively correct the deficiencies identified in any of the FDA mandates. After being given every opportunity to correct their deficiencies, through the legal process a Permanent Injunction was served, permanently closing their doors to future manufacturing. This type of severe legal action on a United States drug company is exceedingly rare. Our review of the evidence confirms the good judgment of the FDA.

A detailed analysis of the cGMP Compliance history of Actavis was performed by the Spyglass Group for the period of 2006 – 2008. The FDA conducted five (5) inspections over this period that resulted in over 40 significant observations and two (2) Warning letters and a final Consent Decree for Permanent Injunction.

In this Expert Report, the SpyGlass Group has classified the FDA observations into five (5) system categories:

1. Quality System
2. Facilities & Equipment Systems
3. Production System
4. Laboratory & Control System
5. Regulatory Requirements

The detailed analysis of the FDA findings determined that each of these systems had numerous observations. There was consistent inadequate corrective action and therefore, there was a pattern of repeat observations. Therefore, critical systems that control the Quality of the product were substantially and consistently out of compliance and operating in a high risk environment. There was no apparent attempt to mitigate the product quality risks through extra testing, inspection, etc.

Digitek/Digoxin double thick tablets were produced from 2004 – 2007. The processes used to produce Digoxin were proven to be unreliable. Management at Actavis was aware of this and other GMP issues but failed to adequately correct the problem. They performed inadequate investigations into the nonconformances; therefore, they were unable to implement sustainable improvements.

Our independent findings have confirmed the FDA issues. Additionally, many more issues were identified that demonstrate that Actavis was critically noncompliant with GMP regulations and released product did not meet GMP.

Actavis management's actions or lack thereof, demonstrates that legal compliance with Federal Regulations as stated in the GMP section of the Code of Federal Regulations was not one of their business priorities. Over at least a six (6) year period, Activis failed to meet legal and patient obligations.

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* Not exhaustive list

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Table of Contents

1. Introduction

The SpyGlass Group, Inc. was contacted by the law firm Motley-Rice, seeking an expert in Quality Assurance and current Good Manufacturing Practice (cGMP)[1] to provide expert opinion in regard to a legal action against Actavis Inc. (formerly known as Amide), a manufacturer of drug products.

Mark G. Kenny & Salvatore J. Romano, PhD have been engaged by Motley-Rice to prepare an expert report, participate in a legal deposition and testify as an expert witness in a trial. Our expert opinion is based upon on over 75 years experience in:

- Running the Quality Assurance and Compliance Programs for multiple medical product manufacturing companies (from small start-up companies to large, multinational companies)
- Objectively and fairly auditing hundreds of domestic and international medical products companies engaged in the development , manufacture and distribution of products regulated by the FDA
- Determining the potential adverse effects that noncompliance has on the product quality and the customer's trust in the product
- Reporting to senior management, risks associated with faulty control systems
- Understanding industry standards commonly used to comply to cGMP
- Reviewing quality records for the purpose of identifying potential violations to cGMP
- Investigating root cause of noncompliance and recommending reliable fix
- Creating effective corrective action programs for many companies in serious violation of cGMP, subsequently eliminating public health risks

[1]

DONE

2. Work Plan

Approach

- Review documented evidence applicable to the scope of the assignment
- Prepare an expert witness report that documents our findings
- Participate in future legal proceedings which may include deposition(s) and a trial process

Quality and Control Systems

- To determine whether or not Actavis[2] was operating within cGMP FDA regulations.
- To determine (through examination of the documents available and a plant visit) whether or not Actavis complied with cGMP and met the requirements for identity, strength, quality, and purity that they purport to have and are fit to be released
- To determine whether or not Actavis released product had a chronic problem with oversized tablet

Product Quality

- To determine whether or not Digitek was released with an oversized tablet problem that might have resulted from deficiencies in their Quality Systems.
- To determine whether or not Digitek (digoxin) tablets made over the period of Nov. 6, 2003 to Nov. 14 2008 meet the requirements for identity, strength, quality that they purport to have and were fit to be released for sale to the marketplace.
- To evaluate various FDA Inspection Results and internal documents associated with the manufacture, test and release of drug products to determine whether Actavis, Inc. was or was not in compliance to applicable FDA Regulations (cGMP), FDA guidance documents and industry standards
- To determine the effect of Activis' compliance performance had on the quality of their drug products
- To determine the likelihood that Actavis had or had not released product that violates FDA Regulations

2

3. Information Utilized

DONE

- Documents gathered by Plaintiffs in the form of FDA reports, 483's, EIR's, Warning Letters, Consent Decrees, and a Permanent Injunction
- Internal Actavis documents such as batch records, investigation reports, memos, & E-mails.
- Depositions of individuals working for Actavis and Mylan
- ~~Plant visit - ??????????????????????~~
- Specific document references are included in the *References* section of this report

4. A Primer on cGMP FDA Regulations & Important Quality Assurance Concepts

What is Drug c GMP?

Current Good Manufacturing Practices (cGMP or more commonly called GMP) is a~~n expertly~~ ~~drafted~~ law that is established in the Code of Federal Regulations. It represents the minimum requirements in the Drug Industry for producing a product that meets all specific requirements for identity, strength, quality, and purity. The law was originally drafted for comment by the FDA using industry acknowledged experts. Industry experts then commented on the content of the draft proposed regulation and in an iterative process, a law was established that outlines the requirements for every drug manufacturer to follow. It has been continually improved (via the same methodology, i.e. industry participation) since its approval in 1978. Our opinion (which is shared by most industry Quality & Compliance leaders) is that it is well designed document and of great help in ensuring that patients and customers receive 100% safe and effective drug products. In fact, most Quality & Compliance leaders place GMP in business terms, frequently refer to GMP as "good business practices." Likewise, it is our experience that the FDA understands our business and fairly and impartially uses a heavy-hand only when they fear public safety. In these high-risk situations, they continually escalate their concerns until all public risks are resolved.

Why is GMP Important?

It is important to understand that the term "Good" is somewhat misleading, GMP is the legal minimum and it is not optional. Our opinion (which is shared by most industry Quality & Compliance leaders) is that significant breakdowns of the Quality and Control Systems (established in this regulation) will inevitably result in serious product quality risks; more specifically, "bad product" being released to the American public.

Why is the FDA Requirement of Investigating and Corrective Action So Important?

All of the controls established in the GMP Regulation are important; however, some are more

important than others. The concept of Corrective Action and Preventive Action (CAPA) is critical.

When errors (referred to as nonconformances) are discovered in any of the Product Quality and/or Control System, by law, industry must investigate the issue. This is common sense to most people, i.e. when you find a problem you need to understand the seriousness of the problem and resolve the situation accordingly. Some nonconformances are important but not urgent. Other nonconformances require immediate investigation, including notifying top management. This practice is somewhat similar to the triage procedure used in a hospital emergency room. For example, if manufacturing equipment were to produce products that had cosmetic issues (e.g. slight crooked printing) of the carton lot number; this is important but not necessarily high risk. The operator has the authority to make an immediate adjustment on the equipment and (with Quality Assurance oversight) inspect the product made, determine when the problem occurred and potentially cull out the defective cases for immediate reinsertion and rework. This type of occurrence would generally not require the immediate notification to top management. On the other hand, if defective tablets (for example double thick) were being discovered at any point in the manufacturing process, immediate actions would result. This is a highly disciplined procedure. It is likely that many of the following actions would be performed;

A. The production line would be stopped and not restarted until a complete investigation was performed (in accordance to a detailed control procedure).
B. This category of defect, i.e. oversized or potentially mixed tablets, creates the highest order of concern for the company. Any suspected suboptimal control system that could result in this type of defect is what keeps Quality Assurance Directors up all night.
C. The Manager of Quality Assurance and Manufacturing would be notified immediately
D. A formal and documented investigation would begin (in accordance to another detailed control procedure)
E. Based upon the preliminary investigation, that lot number would be placed on hold and segregated, identifying the product as potentially defective. Additionally, the batch would be identified in the computer inventory control system as on Hold or Quarantined, thus eliminating any chance for the premature release of the potentially defective product. Classifying the product lot as "On Hold" and later reclassifying a product lot as "Accepted" is a key control step. Quality Assurance is the only one that has the electronic "key" to change these product lot classifications. Unless a worker purposely mishandles defective product, it is almost impossible, in current computer inventory control systems, to generate the necessary paperwork to release a batch for sale.
F. A full-scaled documented investigation would follow, ascertaining the specific (root) cause of the nonconformance. The investigation would extend into many of the control systems within the company, far beyond some of the obvious potential causes. As part of the investigation, a determination would be made as to the acceptability of the batch.
G. After the documented investigation has determined the root cause, a specific documented corrective action program would be designed and deployed.
H. A Material Review Board (or equivalent) would meet to discuss the adequacy of the investigation and appropriate next steps.
I. Ultimately, QA will decide the outcome. Release of product is not a democratic process.
J. Finally, the product would most assuredly be destroyed because they did not have the technology that is sensitive enough to cull out all of the oversized tablets.

What are the Results of Not Following GMP?

There are many potential outcomes, all are adverse. The following identifies a few of these adverse outcomes:

A. FDA Issues - FDA inspections have a reasonable probability to discover the lack of GMP Compliance when problems are more widespread. It is important to understand that no matter how long the FDA spends at the site, they do not have the capability to identify all of the problems. During an inspection, they determine the seriousness of the company's practices and determine the reporting method. When there are issues then the FDA reports the observations using a form – FDA Form 483. Should the situation warrant it, the FDA will continue to escalate their actions from an FDA Form 483 notification to more severe notifications, including: Warning Letter(s), Consent Decree, or worse, including the permanent shutdown of manufacturing (Permanent Injunction). Permanent Injunction is highly rare and represents the FDA's highest order of concern. They are exceedingly rare.

B. Manufacturing Problems – GMP describes fundamental controls that are necessary to be in business. Most of the top companies in the world (regardless of product category) practice these principles and deploy them exceedingly well. Those companies that do not are likely to have significant lapses in sustaining these procedures and are doomed to have product recalls, e.g. Toyota. Companies that experience GMP problems are continually "fighting fires" and are constantly being faced with nonconforming product and nonconforming practices.

C. Product Quality – Product quality will always suffer when GMP is not established. The worse the systems, the worse the problems. Each product defect (originating with complaints, production line, packaging line, etc.) needs to be formally investigated. When a company is constantly fighting these types of fires, there are never enough people to manage the fires. The result is that the problems are ignored or the investigations are superficial, having little chance to determine the root cause and less chance to implement an effective and sustainable corrective action. The lack of effective control systems is the common root cause of almost all product defects. The lack of effective control systems will result in the release of product that does not meet specification, adulterated and are unfit for human use. When this type of product is discovered or the quality is suspect, a responsible company will Recall the product.

What are Some of the Critical Systems & Controls in Drug Manufacturing?

Batch History Record: This is a compilation of all of the vital records and results that provide evidence that the production lot/batch was manufactured and tested in accordance to approved procedures, test methods and specifications. It is also evidence that a batch complies with any FDA submissions. It is a stand-alone document, which means that it should be understood by any experienced reviewer without any significant explanations. It must be complete. The document must include the records previously mentioned plus any exceptions. Exceptions would include issues that were encountered during the manufacturing or testing of a batch. For example the following documentation is required to be in the batch records: out of specification reports, CAPA reports, rework or salvage records, etc. The final control step, before the product is released to market, is the independent Quality Assurance review. This person's responsibility is to review the records of the batch and ensure that it meets specification and was produced and tested in accordance with approved procedures. Quality Assurance then certifies in writing that the product was manufactured and tested in accordance to the approved procedures and the test results meet all

specifications.

Out of Specification Test Result (OOS): If a lab analyst performs a test and discovers out of specification results, then the analyst must follow a strict procedure which involves a formal and documented investigation. The initial first results cannot be automatically disregarded. The strict procedure has built in controls to ensure that the final test results are valid. An OOS is a significant occurrence that requires critical thinking and investigation to properly resolve. The documentation associated with the event must be carefully documented in accordance to the procedures. Failure to follow the OOS procedure will yield results that may be incorrect, ultimately allowing unacceptable product to be released to the market.

Nonconformances: When manufacturing or Quality assurance action does not meet the approved procedure then a nonconformance occurs. When a test is performed and the results do not meet the specifications and/or the documented requirements, then a nonconformance occurs. All nonconformances are required by law to be investigated and handled in accordance to approved procedures to resolve the problem.

Good Documentation Practice: This is an informal term for highly formalized controls. The following highlights some of the more common sense aspects of good documentation practice. All recorded information must be clear, legible and understandable. When an error is made by an associate, the error must be handled in accordance to procedure. There will be signed and approved signatures next to every change of results. There is a legal code of ethics that all information including dated signatures must be honest. All documents requiring approval, e.g. CAPA, must be signed by all of the technical and management associates as required by the procedure. There is no exception to this rule. Any records that are not honest are falsified records. Any unapproved/unsigned and undated documents are not acceptable records and almost unusable. In all steps of the process (raw material receipt and testing, inprocess inspection and testing, product manufacturing and packaging, finished product testing, etc.) Quality Assurance has the responsibility of continually reviewing the records as production progresses. The final Quality Assurance batch history record review is intended to discover Good Documentation Practice nonconformance and hold the batch until a documented investigation is conducted, again in accordance to approved procedures. This is not a nice to do, it is the law. Although the term Good Documentation Practice is not specifically mentioned in this expert report, it is important to understand and have an appreciation for the rules governing records.

Complaint Handling: Each complaint must be properly investigated in accordance to GMP and other FDA guidance documents. This is a disciplined procedure that requires a series of formal events to take place. These steps are intended to determine the potential seriousness of the complaint, the next steps to investigate the complaint and based upon the investigation outcome take appropriate action. The events associated with an investigation may typically include (but is not limited to):

- Examination and chemical testing of the complaint sample
- Examination and testing of product retain sample(s) (retained product samples are required to be selected from every batch and stored in a controlled manner, intended to help investigations into future problems)
- Review of prior complaints with the specific batch
- Review of prior complaints with this specific product and similar products If there is an issue, it must not be automatically be assumed that the problem is only affecting the complaint batch.
- Trend analysis
- Inspection of the Batch Record and other records
- Interviews with manufacturing and Quality Assurance

- Review of studies performed, for example equipment qualification studies, process validation studies
- Review of the adequacy of the current procedures and specifications
- Review of the stability testing results

If the investigation determines that there might be unsafe product in the marketplace, then the investigation must be escalated to top management and a recall decision must be considered. This must be conducted in accordance to procedures and FDA Regulations. Some of the activities and documentation may have to be submitted to the FDA for their review.

5. Expert Opinion

a. Actavis Corporate Culture & Management

There has been consistent evidence that Actavis Management refused to understand the importance of GMP and its direct link to product quality. It appears that their lack of understanding begins at their website[3]. Actavis defines their Manufacturing Practice as based upon GMP which is stated as: "Good Manufacturing Practice (GMP) is a regulatory guideline imposed on all manufacturers of pharmaceuticals…" This statement is not correct because GMP is a Federal Law, not a guideline. This is an important distinction.

Management never displayed an understanding of the legal requirements of GMP. In spite of experiencing significant issues, management never altered their flawed strategy. The significant issues include:

- FDA Form 483
- FDA Warning Letters
- Alarming number of Quality problems
- Product Recalls
- Breakdowns in their Quality System.

They were highly resistive to systematic change, appearing sure that minor improvements would resolve all of their issues. This was a flawed strategy; their arrogance resulted in managing a Drug Company that operated at a high risk level.

This statement by Jacob Haroon (Actavis Management??) (P-147)[4] sent in an email in 2008 describes the situation quite well: "This is all rather sad. Looks like some very basic GMP knowledge was lacking." Unfortunately, it is the Digitek patients that suffered from this troubling situation.

The Corporate culture appeared to place production output ahead of product quality. The CEO said in regard to process validation[5]: " We don't need to practice making tablets"….*(get exact name & quote, & ref.)* It may help to understand that process validation is an FDA mandated controlled study and intended to certify that the process works. This is done by qualifying the equipment and then running a series of batches that are intensively sampled inspected and tested. Since each tablet cannot be individual tested for content and physical quality, there must be a study to validate that operating at the specified conditions always makes good product. Routine sample inspection testing is conducted to provide evidence that the samples (which are considered representative to the entire batch) meet the requirements. If the process is not validated, the sampling technique is an inadequate quality control.

Corporate and QA management were not knowledgeable of the cGMP. Additionally, there was a lack of understanding of the regulatory approval process since many drug products were made and sold without approved NDA's /ANDA's.[6]

In an internal memo[7] (from Wanda Eng dated April 17, 2008 Subject: Totowa Potential 483 Items and Comments) (P-146), provides additional insight into FDA thinking. It is reported that the FDA stated the following serious issues:

- The Quality Unit failed to do its job

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- The Quality Unit has released batches of drug products that failed their specifications
- The Quality Unit failed to adequately conduct deviation investigations in that the root cause was not determined
- Failed to file NDA Field Alerts associated with confirmed stability failures
- Failed to reject products which did not meet in-process and finished product specifications.
- The Quality Unit released products for distribution prior to the completion of the deviation investigation
- Continued to manufacture and ship unapproved DESI drug products after receipt of a Warning Letter requesting justification to market products
- Tested product into compliance and discarded the OOS results; using only retest results without adequate justification
- Failed to have adequate stability programs
- Laboratory investigation of OOSs were inadequate
- Actavis' filings submitted to the FDA to widen specifications when a product fails to meet specification
- Many manufacturing processes are invalidated by the high percentage of stability failures
- Actavis produced digoxin tablets with black spots of unproven origin
- Actavis produced digoxin, a toxic product with double, triple and thin tablets: lots were not rejected

Actavis paraphrased the FDA (P-146)[8] (that were documented by Actavis in full capital letters) as:

- "OUT OF CONTROL"
- "LACK OF RESOURCES"
- "LACK OF EXPERTISE"

The FDA stated in the Warning Letter – E. Main St. – Little Falls – Dated 8/15/2006[9]:

- "Several of the observed deficiencies were long-standing, and there is no indication of how or why the lack of compliance was not identified by your firm"
- "why it was allowed to continue for such an extended period of time"
- "Does your firm have any insight into this situation"?

Mylan stated in the Mylan Audit (M-24) Dated 12/04/06[10]:

- "Shortage of qualified personnel"

Actavis did not respond to the critical FDA observations in the August 2006 FDA 483 in a timely manner (P-137)[11]. Ten (10) months after the 2006 inspection the following was a status of their corrective action implementation:

- 5 not corrected
- 6 partially corrected
- 9 corrected
- 23 total – almost half have not been totally corrected

Actavis Understanding of the Gravity of the Problems

The FDA required that Actavis respond to each adverse notice (483 and Warning Letter). The Actavis letters to the

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FDA represented two areas: 1. Areas promised to correct and 2. Areas that were already corrected. In some ways, they can be thought of as promissory notes and certification of corrective action. Actavis repeatedly failed in this regard. The frequently made promises that were not kept and improvements and corrective actions that were not adequate. After the submission of Actavis' reply to the FDA, there are abundant examples where their reply is not correct. For example, in the Revised FDA Warning Letter – E. Main St. Little Falls - Dated 2/1/2007[12] in regard to Actavis' disagreements with the FDA position, the FDA stated:

- "Your response provides no assurance that the records and conditions of manufacture and testing of each such lot of drug products released and marketed by our firm will be evaluated to assure that the released drug products have their appropriate, identity, strength, quality, and purity
- "In fact, we do not agree with assertions in your August 29 and 30, 2006 letter that certain of the observations listed on the FDA 483 are not accurate"
- "..we are concerned about the quality of the of drug products that have been released from your facility under the serious lack of cGMP controls found during the inspection."

Based upon the continual repeat FDA observations, it is clear that Actavis' replies were incorrect and inadequate. A competent management team would not have allowed these inadequacies to continue.

Lack of Timely Remediation

In the Actavis 5/20/2008 Memo to Senior Management – Summarizing the FDA Inspection (P-106)[13], the FDA inspector stated that "from a Quality Systems standpoint, there was a Total Failure". Additionally, the FDA purportedly stated:

- Do not fix broken systems – get new systems
- (Need) Improved infrastructure
- Investigations on the (past) 483 still not complete
- Health hazards on recalls are delinquent
- We (FDA) get very nervous when you tell us that you are releasing product using current Quality Systems
- One (QA) person was signing off in multiple locations on the batch (this occurred on the Digoxin "double tablet" Investigation). Erin (FDA representative) considered this a very important Observation – additional review of this Investigation may have stopped release of the batch)
- It was "premature to be releasing product"
- The FDA is concerned about product still on the market that was made in Little Falls using similar systems that had failed
- That FDA has concern about the 48 products with no impurity profiles
- The tougher issues are - What is the approach to handling product made under these substandard systems?
- The FDA questioned the validity of Actavis' Batch Record Review process because the FDA had found important nonconformances (e.g. black spots) that were not included in the record. A review of an incomplete batch history record provides a false sense of security.

Quality System Improvement Plan (QSIP)[14] – ACTAV 000484606

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This document is the only evidence that there was ever a systematic attempt to correct the Quality System issues at Actavis. This QSIP was started in the 4th Quarter 2008, three (3) years after the first (in a series) of 483 and Warning letters. Well run firms would have responded immediately after the first 483 in 2006. This would have been an alarm the systems may not be in control and product quality might be adversely affected. These firms would have ordered an intensive internal audit and determined the risk level of each Quality System component. A comprehensive action plan would then be established. In the case of Actavis, it required the hiring of a Quality System consulting firm to begin this evaluation and improvement process three (3) years after the 2006 FDA 483 and 16 years after their first consent decree.

The QSIP identified 201 Observations :

1. Materials Management – 27 Observations
2. Facilities & Equipment – 49 Observations
3. Production Controls - 22 Observations
4. Packaging & Labeling – 15 Observations
5. QC Laboratory – 14 Observations
6. QA – 45 Observations
7. Actavis R&D – 29 Observations

Ineffective Internal Audit Process (P-175)[15]

The Internal Audit Procedure is designed to perform an independent audit of the company's Quality System. It provides management with objective information on GMP compliance. Many of the problems associated with the FDA issues should have been identified through the internal audit procedure and formally communicated to management.

A review of an internal audit (conducted on 1/24/08 identified 17 issues, most of which here highly specific to procedures and records. There is no evidence that the auditor identified any of the systemic issues that were later identified by the consultants in the 4th Quarter of 2009. It would not be expected that an audit would find all of these observations; however, many of the fundamental issues should have been identified as requiring improvement. Management did not understand the criticality of an objective review and apparently assigned it to an inexperienced associate.

SpyGlass Group Summary

The aforementioned issues indicate the gravity of their situation. Actavis did not appear to have the ability and experience to run a drug manufacturing business. In fact, they appeared to lack the knowledge and the intuition to know that they didn't have the ability to manage a drug manufacturing business. It was only in the very late stages of the company's life cycle that they finally realized that they needed outside experts (in the form of a team of qualified consults); unfortunately, it was too late to correct the nonconformances and avoid a Permanent Injunction.

Clearly, the issues indicate that an effective Quality System was never achieved. Their legal obligations were never fulfilled. It is highly disturbing that there was a lack of understanding and urgency to these serious issues. It is difficult to understand how a company that experienced a Consent Decree on 03/25/92 failed to implement any kind of sustainable compliance to GMP.

15

b. Product Quality & Quality Systems

This section of the report analyzes some of the situations related to Product Quality Nonconformances, Deviations and OOS. It is our opinion that many mistakes in judgment were made. These mistakes in judgment resulted in the release of defective product. Had there been experienced management, these problems would have been handled correctly.

The following highlights some of the major Product Quality issues and the alarming rate of OOS, Investigations and Deviations:

1. There were multiple incidences of Double Thick and Overweight Digoxin Tablets:
   - 2004 Complaint Report of Double Thickness 0.25 mg Digoxin Tablets (Lot #3611A)[16] See detailed analysis that follows.
   - 2007 Investigation of 2nd Report of Double Thickness Tablets (Lot #709241)[17] See detailed analysis that follows.
   - Digoxin Tablets (Lot 80202A1) (M-16)[18] – Bulk tablet lot was released to filling and packaging only later to be placed on Hold due to tablet weights
   - Digoxin Tablet (Lot 80228A1) (*P-63 FDA Request for Soft Tab High or Low Weight Investigation (P-63 memo from Lisa Bennet dated 2/25/2009) (P-141??)*[19] – This lot had a tablet weight problem that was "Discovered in Packaging" (INV 08-060)
   - Digoxin Tablet (Lot 70148A) ????
   - Digoxin Tablet (5453A) (P-133 XXXX) ???
   - Others??????
   - Check APRs
2. 2007 Lab OOS - There were over 100 reported OOS within the QC Laboratory for 2007. A total of three (3) were specifically for Digoxin. *QC Laboratory 2007 OOS (Log) (Document 3006414)*[20]
3. 2007 Lab OOS - There were over 100 reported OOS within the QC Laboratory for 2008. A total two (2) were specifically for Digoxin. There was no apparent improvement when compared to the prior year. *QC Laboratory 2008 OOS (Log) (Document 3006420)*[21]
4. 2007 Investigations - There were over 100 Nonconformances that required a formal documented investigation. A total of three (3) were specifically for Digoxin. *Investigation Log 2007 (Document Number 3005608)*[22]

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5. 2007 Investigations - There were over 224 reported Nonconformance that required a formal documented investigation. A total of ten (10) were specifically for Digoxin. There was no apparent improvement when compared to the prior year. *Investigation Log 2008 (Document 3005503)*[23]

6. 2008 – 2009 (12 month period) Deviations - There is a 59 pages summary report that lists the Unplanned Deviations that were conducted from 12/5/08 – 11/10/09 (12 month period). There were a total of 247 unplanned deviations. Unplanned deviations are initiated when a batch/material/procedure is nonconforming/OOS and management determines that they wish to accept the nonconformance/OOS and continue to process the product, ultimately for release to the market place. *Deviation List Report (Log) (Document 3005547)*[24]

7. 2006 – 2007 Rejections (17 month period) - There were approximately 20 batches rejected. This number is alarming, but not unexpected due to the high number of OOS, Deviations, and nonconformances over the same period of time. *Rejected Batches from August 2006 through 2007 (17 months)(Document 5475428)*[25]. The greater issue is not the number of rejected batches (since these were caught) but the potential that other batches (that should have been rejected) were released for sale.

8. 2007 – 2008 OOS (8 month period) *(P-210)*[26]– There were a total of 96 OOS results that were recorded during the period of 9/07 – 4/08. This is an extraordinary number of OOS. Extrapolated out this number will exceed 125 OOS results annually. During this eight (8) month period a total of nine (9) OOS involving 14 Digoxin lots. The OOS results were in multiple manufacturing and control areas:
   - Lot 70924A1 – a double thickness investigation resulting from discovery of thick tablets at packaging (the compression process passed along OOS tablets)
   - Lot 80044A1 – a stainless steel screw was found in tablet well during packaging (the compression process, which includes metal detection, did not detect the presence of a huge metal particle)
   - Lot 80051A – Spots on tablets
   - Lot 80053A – Did not record metal detector and there is no record that the lot was reprocess through the metal detector
   - Lot 70078A1 – Zero stability not recorded
   - 80108A – QA inspector verified wrong incorrect bar code
   - 800152A and 080154A – Process Validation protocol issues
   - 80133A – Operator notice that tablets were thinner during a routine inspection of a finished drum
   - 5 different batches – Process Validation protocol issues

9. Blending OOS - There were a total of 19 lots with product blending OOS. (*Batch Blending Failure Out of Specification, P-183, and Email from Wanda Eng dated 7/20/2007)*[27]. As a result of the investigation, 6 lots were rejected, 6 were released for sale and 8 were still on hold (as of 7/20/2007)

   This number of blending nonconformances should have triggered a systematic review of the blending processes and then questions whether or not the processes are adequately validated. It should be noted that two (2) of the lots are Digoxin. One was released for sale. By contrast, most pharmaceutical operations have few if any blending OOS; however, if they occur, a comprehensive investigation and CAPA is implemented.

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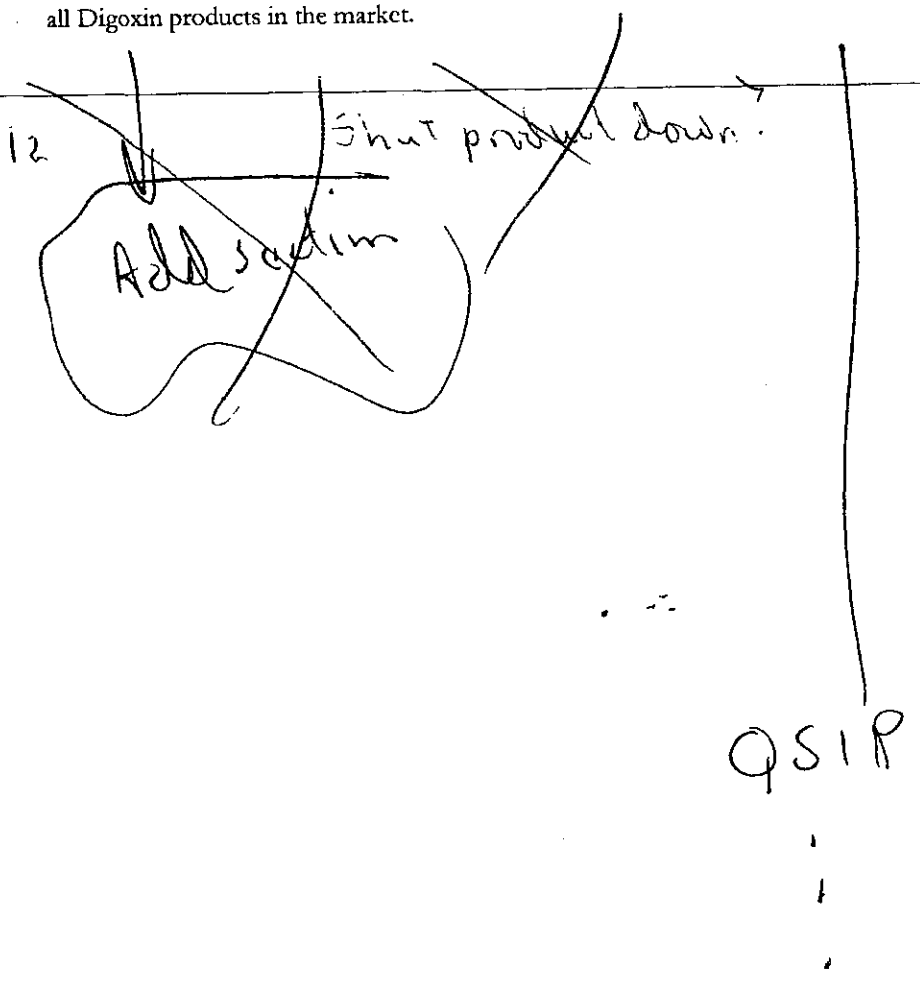
10. Investigation Review Board – (P-216) [28]– On March 23, 2008 there were 53 open investigations into OOS. A total of 28 investigations into OOS were open for more than 50 days. Many were open for more than 100 days. The number of investigations is concerning; however, their length open is more concerning. Investigations of OOS must be completed quickly because for several reasons. The longer the wait, the less probability that the root cause can be determined. Even more important is that this lengthy investigation has the potential to impact a much greater scope (than the specific batch of raw material or product). For example, if the OOS investigation determines that a commonly used instrument is not providing accurate results, then the effects of this faulty equipment must be determined. If an investigation is done at day 100, then all of the tests conducted using this equipment is suspect. The investigation into this type of event would be highly difficult and potentially widespread.

11. Product Recalls – The nonconforming product was of sufficient risk to the public to warrant the recall of all Digoxin products in the market.



28

Review of 2004 Complaint Report of Double Thickness 0.25 mg Digoxin Tablets (Lot #3611A)

Investigation No: 04-003 –Complaint Investigation Final Report

Digoxin Tablets 0.25 mg
Lot 3611A

FINDINGS

Investigation Report 04-003[29] summarizes the results from a customer complaint received by Actavis on 7/7/04. A pharmacist returned a 0.25 mg Digoxin tablet from Batch # 3611A which was approximately twice normal thickness and weighed twice as much. The investigation of the process records showed nonconformances. Two Stokes compression machines were used on Batch # 3611A. Under normal operation these machines cannot make double thickness tablets. Upon machine set up however, double thickness tablets can be made. In this case double thickness tablets are observed by the set up operator who adjusts the machine and thinks he/she cleared the area of any double thickness tablets prior to actual production startup. QA's inspection did not detect the defect. The compression operation begins and lasts for several days until the bulk blended batch is exhausted. QA then continuously monitors the quality of the product and conformance to procedures. The batch size target is about 4.8 million tablets and a single batch of digoxin tablets can take several days to compress.

Investigation 04-003 concluded the most probable cause of double thick tablets was that they were made during the initial setup, the single tablet returned became stuck in the deduster and was not removed or detected prior to starting the production run.

The following identifies some of the serious issues with the actions and documentation associated with Complaint Investigation Report 04-003

- Approval by Top Management: - The Investigation Final Report is not signed and dated. The Investigation Final Report was never approved by Senior Management as required by the SOP. The SOP requires the following management approvals:
  - Quality Assurance Director
  - Vice President Scientific Affairs
  - Manufacturing Operations Director

  This is a serious violation of cGMP. An undated and unapproved/unsigned document does not provide formal/legitimate evidence that the right things were done.
- Corrective Action Dates – There are no dates associated with the corrective action
- Analysis of the Complaint Sample: There was no analytical testing of the complaint sample
- Critical Corrective Action - Verification of corrective action is documented; however, records of the Production and QA Departmental Operating Procedures indicate that not all of the corrective action was implemented as stated. One of the few stated corrective actions required that the manufacturing

29

operators will clear the dedusters by operating the dedusters at the maximum vibration setting. There is no evidence that the SOP's were updated to reflect this change in operating procedure.

- Unapproved Records - Records critical to the investigation and corrective action are not approved and are not dated. Unapproved and undated records are in violation of good documentation practice elements of the GMP and are not considered valid.
- Undisciplined & Inadequate Investigation – The investigation does not follow any generally accepted problem solving approach or method. The root cause was never identified, yet the investigation only focused on cleaning the deduster and chutes at start-up. There are many more potential root causes that were not considered.
- Inadequate Investigation and Corrective Action – The corrective action was not effective as was evidence by a repeat double thick tablet incident (Lot 709241A1/A2)

SPYGLASS GROUP SUMMARY

Actavis demonstrated general incompetence in the handling of this critical product quality. Had the proper investigation been performed, a root cause would have been determined and the weak links in their practices might have permanently resolved the double thickness matter. In 2004 Actavis released product with serious defects. Actavis response to this serious issue was not adequate and the actions did not comply with the GMP Regulations. The complaint samples might have been double or more of the labeled dosage. Based upon the lack of GMP controls in place at the plant, there is no reason to believe that this was an isolated incident. The investigation performed was inadequate; therefore, the problem was likely to resurface. The same problem did resurface in 2007.

There were critical quality issues identified at almost every point in the production, control and testing processes. Actavis consistently released defective product, including Digoxin. There was a breakdown in their Quality Systems that allowed mistakes and errors in judgment to occur. It is our experience that good people don't come to work with the intention of doing a bad job. It is the company's environment that fosters bad behavior. The Actavis environment was not focused on GMP and Quality Systems.

2007 Investigation of a 2nd Report of Double Thickness Tablets (Lot #709241)

Investigation Log No 07[30]
Digoxin Tablets 0.125 mg (145)
093Lot 709241A1/A2 (A1 is the original packaged batch, A2 is the 100% inspected and salvaged batch)

DISCUSSION

The chronology of the events associated with the double thick Digitek tablets is as follows:

The double thickness Digitek problem surfaced again on 11/30/2007 when five (5) double thick tablets were discovered while in the middle of packaging the lot. Packaging continued with the QA instructions "If one or two thick tablets found, continue packaging operation with a watchful eye." During the packaging a total of 5 additional double thick tablets were found in drums 15/16, 17 and 34. On 12/04/2007 this packaged batch was release for sale. On 12/05/2007 this batch was placed on hold by QA. On 1/11/2008 the batch was salvaged by through 100% visual inspection. On 1/22/2008 the lot was sampled by QA, no additional tablets were found. On 1/23/2008 the inspected batch was approved for packaging. On 1/28/2008 the batch was approved by QA. See the batch chronology in Attachment XX

FDA issued a 483[31] on an inspection of 993 Riverview Drive from an audit from 3/18/08 to 5/20/08 with 11 major observations. Observation 2 states that " Drugs products fail to meet established specifications and quality control criteria are not rejected." Specifically it states in 2 a. " During packaging of Digoxin Tablets 0.125 mg, lot #70924A1, five double thick tablets were observed. Quality Assurance approved a 100% visual inspection of the 4.8 million tablet lot which resulted in an additional 15 double thick tablets. Although Quality Assurance was aware of the "double thick' tablet findings, the batch was then released based on AQL sampling which included visual inspection of 1330 tablets. No root cause was determined for the defect; however the lot was released to the market by the Quality Unit on 1/28/08 following the visual inspection. There was no documented evaluation of the approximately 89 lots remaining on the market at the time of inspection." The FDA had grave concerns about all 89 lots that were released for sale to the public. The facts of this situation ended with a mandate for full product recall.

There are many issues associated with the handling of the double thickness issue.

Unexplained Decisions

30

31

2007 Investigation of a 2nd Report of Double Thickness Tablets (Lot #709241)

- When the defective tablets were later discovered in packaging, the packaging operation was allowed to continue. The operation should have been immediately halted. All products made to that point should have been immediately placed on hold and properly labeled as such. There should have been no further processing until a comprehensive investigation was conducted.
- On 12/4/2007 uninspected finished product lot containing defects was released for sale by Quality Assurance. A day later (12/05/2007), QA reversed their decision and decided that the batch was not acceptable and should not be distributed. How could an event like this occur in a well controlled environment? This is a breakdown of the highest order. The distribution of the lot was halted and the product lot was placed back on hold without any documented reason for this action. This incident alone should have classified as a nonconformance and properly investigated, including a potential CAPA. The batch was subsequently salvaged by breaking down the package, saving the tablets, visually inspecting the lot to eliminate defects, repackaging and then re-releasing the salvaged batch. The justification for these actions was not documented.

Inadequate Quality Problem Investigation

- Root cause of the problem was never confirmed but "appeared" to be caused at compression machine startup.
- Tablet compression was on 2 Stokes Presses over a 3 day period. The presses were stopped a total of 18 times for breaks, lunch, and overnight with very few QA checks on restart. Stoppages ranged from 20 minutes to 17 hours.
- Actavis identified the lack of cleaning of the deduster at compression startup as the most probable root cause; however, records indicate that this may not be correct. A total of 20 double thick tablets were found in the batch. Their investigation determined that they only opportunity for this to occur was at compression startup. This conclusion may be flawed. Five (5) tablets were found in the first inspection process in buckets #15 &#16 (2 tablets within both buckets), #17(1 tablet), and #34(2 tablets) and in 100% inspection another 15 with no locations noted. This indicates that the problem occurred throughout tableting or original filling process and not just at startup. This information was never even considered during the root cause analysis. Again, how could these all be the result of startup when they were spread throughout many buckets?
- Investigation is incomplete and never included other potential root causes to the production of double thick tablets, including:
  - There is no documented investigation into complaint history for similarly manufactured tablets
  - Double thick tablets were never chemically tested. The dose of the double tablets is not known.
  - No review of records to determine if the equipment is qualified and the process validated
  - No review of the training records of the associates
  - No consideration of design changes to the equipment to eliminate future defects
  - No review of the proper use of defect buckets and labeling practices
  - No detailed review of the history of this type of nonconformance
  - No clear conclusions resulting from the investigation
  - No investigation into the history of changes to the equipment
  - No review of the preventive maintenance of the tableting equipment
  - No review of the other lots of Digoxin tablets within their control or on the market which could exist
- There was no subsequent increase in QC checks or other controls (intended to add further capability to detect double thickness tablets). Some steps should have been implemented to mitigate the risk

2007 Investigation of a 2nd Report of Double Thickness Tablets (Lot #709241)

since the root cause of the problem was never determined.

Ineffective and Unreliable Methods to Salvage a Known Defective Tablet Batch

- Production and Quality Assurance used a method to salvage a defective batch (containing double thick tablets) that is generally not accepted in the drug industry as being effective, i.e. their method for attempting to cull out 100% of the defects within a 4,800,000 tablet batch through human 100% visual inspection. This method of visually inspecting out defects is known throughout the medical products industry to be unreliable[32]. It is frequently quoted within the industry that 100% inspection is no better than 80% effective. Said another way, 100% Inspection is not 100% effective. Based upon this industry accepted understanding, it is almost certain that further defective tablets remained in the batch. (Ref. Juran and Craig QP 2004 July)

- After 100% inspection, the batch was subjected to another QA inspection using a tightened AQL where each of the 34 individual buckets from the batch was randomly sampled[33] with 40 tablets each. After visual inspection, a Quality Control sample inspection was designed to allow less than 100% effectiveness. The batch could be released even if a defect was found in the final QA samples (i.e. the lot would pass if one (1) defective tablet was found in the samples, only rejecting if two (2) or more defective tablets were found.) The "tightened " AQL testing plan would have released the batch even if one defective tablet were found. What was QA and Management thinking?
- There is no documented procedure that describes the equipment, techniques and methods used in the 100% visual inspection.
- There was no Quality Assurance monitoring of the visual inspection.
- There is no documentation that the inspectors were properly trained on the inspection method
- The salvage method was not properly approved. There was no approved Deviation Record to authorize the procedure of tearing down finished product and 100% inspecting.
- There is no record that the visual inspection procedure is effective. The procedure was never qualified.
- The acceptance criteria for 100% inspection were not established. How thick was too thick?

Inadequate Batch Record Detail of the Lot Salvaged Through 100% Inspection

- There is no documented evidence that the defective lot was properly salvaged. For example, the following required information was not included in the batch record:
  - Inspection Start and End Date/Time
  - Name and document number of the 100% inspection procedure/method
  - Startup inspection
  - Clean up inspection
  - In-process Quality inspection monitoring
  - Inspector's names
  - Inspector's training records
  - Deviation authorization number
- The inspection protocol did not include the required information, for example:
  - Inspection Procedure

[32]

[33] Sampling Plan - The sample and test plan was as follows: AQL level = 0.065, Sample Plan= single, tightened level 1, Sample Size Code = Q, Bulk Size ~ 4.8 million, Inspect 1250 tablets minimum from 34 drums. 40 from each of 33 drums, 10 from 34th drum. Tablets taken at random, Accept on 1/reject on 2 of total batch

2007 Investigation of a 2nd Report of Double Thickness Tablets (Lot #709241)

- Acceptance Criteria and Specifications
- QC Sampling Plan
- Responsibilities

- All of the activities were handled according to incomplete and disjointed memos and apparent verbal instructions.

SPYGLASS GROUP SUMMARY

- Batch # 70924 should have been rejected and destroyed. There is no confidence that the process was capable of producing defect free tablets. The methods and procedures in place during the production of Lot 709241A were not in compliance to FDA GMP Regulations. It is not possible to defend management's action in this regard.
- Significant violations of GMP contributed to the production of a lot containing critical defects, i.e. "double thick tablets".
- After the discovery of tablet defects, the lot was not destroyed. In fact, there appeared to be continuous waffling back and forth in terms of the correct disposition of the batch.
- In the attempt to salvage 4,700,000 tablets, the defective batch was further processed using ineffective and unvalidated methods that would not have provided a high level of assurance that the lot was defect-free. Among the unvalidated methods, a human 100% inspection process is not effective and will not remove all defective, especially in such a large batch. It was in some ways like trying to find a needle in a haystack. The nonconformance investigation never conclusively determined the root cause of the problem.
- The investigation was not thorough and comprehensive or in accordance to the regulatory requirements.
- Because the investigation was inadequate, the corrective action may not be effective in preventing recurrence of the double thick tablets.
- In regards to the double thickness quality problem, the records demonstrate that Actavis knew the problem existed from at least 2004. We challenge the wisdom in the decision to release Digitek, digoxin 0.125 mg , Batch # 70924 for sale. We challenge the decision not to reject and destroy the batch. As with many other nonconformance, deviations and OOS, a root cause determination was not evident and the corrective action to prevent recurrence was either not effective or never implemented. An experienced Quality Assurance Head would not have followed the Actavis decision making path.

c. Actavis FDA Observations and Events

The Federal Government cited Actavis for serious GMP violations in 5 FDA inspections over a period of 2006 to 2007 issuing a Permanent Injunction on 11/12/08. This Injunction shut down all production and sales of products from all of their NJ locations.

FDA records demonstrate that there were unacceptable and noncompliant practices for a six (6) year period. An analysis of the FDA 483's, Warning Letters and Consent Decree confirm that there were repeated nonconformance in the fundamental control systems; including,

- Quality System
- Facilities & Equipment System
- Production System
- Laboratory System
- Regulatory Requirements

The observations are summarized in *Attachment D – FDA Observations & Events.* A review of this document will confirm the pattern of repeat nonconformance.

The following summarizes some of the :

Quality System

The FDA identified Quality System issues in every 483 report. The observations included:

- Changes made to records without approvals
- Inadequate investigations of complaints
- Inadequate investigation of nonconformances
- Failure to prevent the release of lots with significant nonconformances
- Batch failures not investigated

Facilities & Equipment System

- 25% of the manufacturing equipment is not qualified
- Inadequate preventive maintenance program
- Equipment qualification issues

Production System

- Lack of Cleaning Validation
- Production documentation not controlled to protect unauthorized changes
- Inadequate inprocess testing
- Deviations from production and process control
- Records not complete
- Inadequate storage practices
- Procedures not followed

Laboratory System

- Stability Testing Protocol not followed
- Unsecure computer records
- Quality testing records incomplete
- Changes to lab notebooks after it was approved
- Original OOS results not recorded
- Lab computer system is not validated
- Examples where products did not meet specification throughout the product's shelf life
- Lab controls that are not scientifically sound

Regulatory Requirements

- Adverse Drug Experience (ADE) information not reported to the FDA
- ADE not investigated
- Procedures not established for post marketing ADE
- Field Alert Reports not submitted on time

A review of this attachment will also confirm that serious violations occurred, including the release of Digoxin that failed to meet established standards and specification and other relevant quality control criteria. As a result of the FDA concerns, a complete recall of all Digitek lots was conducted.

This repeat pattern of serious violations to GMP, the release of nonconforming product and the FDA's intolerance to the continuation of this unacceptable public risk, resulted in a court ordered permanent closure of the plant.

d. Place Keeper

12. References

- **References & List of Documents Utilized**
- (this needs to be organized better….need to number them and them list them in the text with the appropriate #)
- Digitek Digoxin Tablet – Documents to support opinion
- 7/9/04 Plaintiffs Exhibit # 128, Amid Pharma Investigation Report # 04-003. Complaint of double thick 0.25 mg tablet.
- 1/10/06 Plaintiffs Exhibit #79, FDA 483, observation # 8 on compression problems.
- 8/15/06 Plaintiffs Exhibit# 35, FDA Warning Letter, ADE's and no ANDA's
- 2/1/07 Plaintiffs Exhibit# 25, FDA Warning Letter, revision of # 35
- 4/07 ???? Plaintiffs Exhibit# ???, APR 2007 for 0.125 mg Digoxin including Batch # 70924 as being released
- 11/12/07 ?? Plaintiffs Exhibit# ??? Batch Record # 70924
- 12/5/07 Plaintiffs Exhibit# 16, Investigation Report #07-093, Batch # 70924, double thickness
- 3/18/08 Plaintiffs Exhibit# 26, FDA 483 , Batch # 70924 etc.
- 3/18/08 Plaintiffs Exhibit# 91, FDA EIR, inspection of 8/18 to 5/20/08.
- ??? 2008 Plaintiffs Exhibit# 144, APR 2008 0.125 Digoxin.
- 11/14/08 Plaintiffs Exhibit# 82, Complaint of Permanent Injunction.
- Quality Control Handbook, J.M.Juran, 3rd Ed. , 1951, McGraw-Hill, pp. 12-61 to 12-63. On 100% Inspection Accuracy.
- Quality Progress, D.J.Craig, July 2004. On 100 % Inspection Accuracy.

13. Appendices

Appendix A – SpyGlass Qualifications

Appendix B- Chronology of Lot 70924 – Double Thick Lot

Date	Action
11/12/2007	Digitek Lot Number 70924A was started – Theoretical batch size of 4,800,000
11/16/2007	Tablet Compression Machine was set up
11/17/2007	Started Compression (one operator was running 2
11/18/2007	Finished Containers 1 – 14
11/19/2007	Stopped, removed and cleaned upper and lower punches due to excessive build-up of powder (press 67)
11/19/2007	Finished Containers 15 – 26
11/20/2007	Finished Containers 27 – 34 (final container)
11/29/2007	Packaged 4.754 million tablets
11/30/2007	Two tablets found on line #405. Two prior buckets inspected with no additional double thick. Packaging resumes. QA instructed "If one or two thick tablets found, continue packaging operation with a watchful eye". A total of 5 double thick tablets were found. (buckets 15/16, 17 and 34)
12/01/2007	Competed, found "only" one tablet from Bucket # 17
12/01/2007	Finished stock transfer sheet completed to move product into accepted status
12/04/2007	Finished product approved and formally released by QA
12/05/2007	Batch placed on hold
1/11/2008	Bitler issues Inspection Protocol authorizing 4,722,000 tablets to be inspected
1/18/2008	Repackaged batch passed the reinspection requirements (a total of 15 double thick tablets were found during 100% inspection)
1/21/2008	QA Sample Inspection protocol issued
1/22/2008	QA Sample Inspection completed – no double thick tablets found in sample
1/23/2008	Ashesh Dave issues email stating that the line operator found thick tablets previously at packaging and is requesting to repackage the lot
1/23/2008	Finished product acceptable
1/24/2008	Packaged 4.754 million salvaged tablets
1/24/2008	Ponzo issues an investigation summary
1/25/2008	Batch accepted/authorized for repackaging (Dan Bitler approved) AFTER repackaging
1/28/2008	Lab results indicate acceptable
1/28/2008	Batch released
1/30/2008	Batch shipped

Appendix XX – Place Keeper

Appendix D – Summary of FDA Observations and Events

EVENT & LOCATION	QUALITY SYSTEM	FACILITIES & EQUIPMENT - SYSTEM	PRODUCTION SYSTEM	LABORATORY & CONTROL SYSTEM	REGULATORY REQUIREMENTS
FDA 483 – E. Main St. Little Falls, Dated 12/1/04 P???	- Changes made to records without approval (2) examples	- 25% of the manufacturing equipment not qualified (6) examples	- Lack of Cleaning Validation (2) examples - Production documentation is not controlled to prevent unauthorized changes (3) examples	- Unsecure computer records (3) examples	-
1. **FDA 483 – E. Main St. Little Falls – Dated 2/8/06 P-79** **7 Observations**	- Inadequate investigation of complaints – three (3 examples - Inadequate Complaint Procedure -	-	- Control procedures are not established to validate the performance of manufacturing processes – two (2) examples	-	- Adverse drug experience (ADE) information has not been reported to the FDA - Adverse drug experiences not investigated - Adverse drug experience information not reviewed - Some ADEs were not reported to the FDA - Procedures not established for post marketing ADEs
2. **FDA 483 – E. Main St. Little Falls – Dated 8/10/2006 Exhibit 8** **15 Observations**	QA failed to prevent the release of lots that had significant nonconformances, including: - Incomplete lab data - Batch that failed to meet specification - Batch record deviations - Manufacturing deviations QA filed to detect significant discrepancies in Quality reports and records, five (5) examples include.	- Examples of inadequate equipment preventive maintenance program	- Inadequate validation of the cleaning procedures for manufacturing equipment - Inadequate inprocess testing for four (4) examples - Deviations from production and process control procedures not justified for three (3) examples - Master product and control records are incomplete - Equipment qualification issues	- Seven (7) different product Quality Testing records were incomplete – Examples. - Changes entered into lab notebooks after it was approved - Original out of specification results for three (3) different products were not recorded - Lab computer system was not validated -	

EVENT & LOCATION	QUALITY SYSTEM	FACILITIES & EQUIPMENT - SYSTEM	PRODUCTION SYSTEM	LABORATORY & CONTROL SYSTEM	REGULATORY REQUIREMENTS
	- Stability testing - Process Validation - Batch record Batch failures not investigated - Stability testing - Lab testing - Active ingredient uniformity of tablets Stability Testing Protocol not followed -		- Rejected in-process are not identified and controlled properly - Inadequate storage practices for chemical raw materials - Chemical raw material handling procedure not followed		
3. **Warning Letter – E. Main St. – Little Falls – Dated 8/15/2006 P-229**	FDA stated that Actavis. - "Several of the observed deficiencies were long-standing, and there is no indication of how or why the lack of compliance was not identified by your firm" - "why it was allowed to continue for such an extended period of item" - "Does your firm have any insight into this situation"? - Prior response to the FDA does not include details that were discussed during the inspection." - Prior response does not identify the cause of the observed deficiencies with regard to postmarking reporting requirements				
4. **FDA 483 – Taft Road – October 2006** **3 Observations**	-	-	-	- Deviations not justified - Test Methods not properly validated - Suitability verification not conducted	-
5. **Mylan Audit Dated 12/04/06 M-24**	- Shortage of qualified personnel	- Dated equipment - Warehouse leaking water - Ventilation system smelled of mildew	-	- Quality Control Lab congested	-
6. **Revised Warning Letter – E. Main St. Little Falls - Dated 2/1/2007 P-25**	- Summarized the prior observations and emphasized the seriousness of the noncompliant observations - Actavis Corrective Action and is in disagreement: o FDA stated "In fact, we do not agree with assertions in you August 29 and 30, 2006 letter that certain of the observations listed on the FDA 483 are not accurate" o " .we are concerned about the quality of the of drug products that have been released from your facility under the serious lack of cGMP controls found during the inspection." o "Your response provides no assurance that the records and conditions of manufacture and testing of each such lot of drug products released and marketed by our firm will be evaluated to assure that the released drug products have their appropriate, identity, strength, quality, and purity				
7. **FDA 483 – E. Main St. Little Falls – Dated 9/28/2007 P-50**	-	-	- Approved production and process procedures not followed	- Stability Testing Protocol not followed	- FDA required – Field Alert Report not submitted on time

EVENT & LOCATION	QUALITY SYSTEM	FACILITIES & EQUIPMENT - SYSTEM	PRODUCTION SYSTEM	LABORATORY & CONTROL SYSTEM	REGULATORY REQUIREMENTS
8. FDA 483 – Riverview Drive – Dated 5/20/2008 P-26	- Procedures not followed - Responsibilities not followed - Released products not meeting specifications - Four (4) examples of not investigation products out of specification results - Four (4) examples of inadequate investigation into unexplained discrepancies	-	-	- Eleven (11) examples where products did not meet specifications throughout the products labeled shelf life - Five (5) examples of lab controls do not include scientifically sound test procedures	-
9. Actavis 5/20/2008 Memo to Senior Management – Summarizing the FDA Inspection	FDA Inspector stated "One person was signing of in multiple location and the batch (this occurred on the Digitek double tablet Investigation – The FDA Inspector considered it a very important Observation – additional review of this Investigation may have stopped the release of the batch FDA inspector stated that "from a Quality Systems standpoint, there was a Total Failure". Issues and needs (from FDA inspector). - Do not fix broken systems – get new systems - (Need) Improved infrastructure - Personnel - (Need) Philosophical Change - Investigations on the (past) 483 still not complete - Health hazards on recalls are delinquent - "Get very nervous when you tell us that you are releasing product using	-	FDA inspector stated that. - "premature to be releasing product" - "concerned about product still on the market that was made in Little Falls using similar systems that had failed" - "concern about the 48 products with no impurity profile"	-	-

EVENT & LOCATION	QUALITY SYSTEM	FACILITIES & EQUIPMENT - SYSTEM	PRODUCTION SYSTEM	LABORATORY & CONTROL SYSTEM	REGULATORY REQUIREMENTS
	current Quality Systems -				
10. Consent Decree for Permanent Injunction Exhibit 214	- Inspected the firms facilities in Totowa, Little Falls and Taft Rd a total of eight (8) times The FDA stated: - "drugs are adulterated" - "Interstate commerce drugs that are misbranded" - Introduce or deliver "new drugs that are neither approved" per regulations - "FDA's five inspections of Actavis Totowa's facilities over the last three years have revealed numerous and recurring violations of the current cGMP requirements for drugs"				
Depositions	-	-	-	-	-
	-	-	-	-	-
	-	-	-	-	-
	-	-	-	-	-